

## **Pseudoxanthoma elasticum (PXE) patients and heterozygous carriers have decreased plasma PPi levels which correlate with the (cardio)vascular phenotype.**

M. Van Gils<sup>1,2</sup>, J. Depauw<sup>1</sup>, S. Verschuere<sup>1,2</sup>, L. Nollet<sup>1,2</sup>, O.M. Vanakker<sup>1,2</sup>

1. Center for Medical Genetics, Ghent University Hospital, Ghent, Belgium

2. Department of Biomolecular Medicine, Ghent University, Ghent, Belgium

### Introduction

In pseudoxanthoma elasticum (PXE) patients, decreased levels of inorganic pyrophosphate (PPi) are associated with occurrence of ectopic mineralization. Thus far, no data are available on PPi levels in heterozygous carriers nor is it known whether a correlation exists between PPi levels and the *ABCC6* genotype and phenotype of patients.

### Methods

PPi was measured in 106 citrated blood samples (71 from 42 PXE patients, 21 from 20 carriers and 14 controls) via ATPase luminescence assay. Phenotyping was done using Phenodex scoring (PS). Correlations between PPi, PS, age and sex were analyzed via Spearman's correlation analysis. Genotype correlations were assessed using ANOVA between 3 mutation archetypes: erroneous mRNA transcript (D: deletion, frameshift, splicing), nonsense (N) and missense (M) variants.

### Results

Compared to controls, patients and carriers had respectively 49% and 20% less PPi ( $P < 0.001$ ), though overlap existed between the groups. In patients, PPi was significantly lower in males compared to females ( $P < 0.05$ ). PPi levels were not influenced by age but inversely correlated to vascular PS ( $P < 0.05$ ), with a near-missed significant correlation to the cardiac PS. No correlation was found with skin or eye symptoms. A significant difference in PPi levels between D+M and N+M clusters was found ( $P < 0.01$ ).

### Conclusion

PPi plasma levels are significantly decreased in patients and carriers, influenced by sex and genotype. Though unrelated to age, skin and eye disease, the PPi levels are inversely correlated with (cardio)vascular burden in PXE patients, making PPi promising as a cardiovascular biomarker in PXE.